

## Case Report

### Facial Features and Iron Overload Detected in Buccal Smears of Thalassemia Patient: A Case Report

Naga Mahita V, Manjunatha BS, Rina Shah, Suresh Kovvuru, Sharad Purohit, Arun Kumar Reddy Vangala

#### Abstract

Thalassemia is a group of genetically inherited disorder of hemoglobin characterized by reduced synthesis of the alpha or beta chain of globins. Conventional treatment of  $\beta$ -thalassemia major is regular blood transfusions to keep the hemoglobin levels close to normal. Iron overload is common among transfusion-dependent patients who do not receive effective iron chelation therapy. Liver biopsy and bone marrow biopsy are widely followed definitive tests for assessing iron overload. These procedures are however invasive and may not be feasible in every occasion. A 10 year old  $\beta$ -thalassemia child presented with carious lesions undergoing blood transfusions wherein iron overload was detected by using a simple non-invasive buccal smear stained by Perl's Prussian blue stain.

**Keywords:** Anemia; Blood Transfusions;  $\beta$ -Thalassemia Major; Cytology; Hemosiderosis; Iron Overload.

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#### Introduction

The  $\beta$ -thalassemia is a hereditary blood disorder that results in a failure to produce  $\beta$ -globin chains, and as a consequence, normal hemoglobin cannot be synthesized. In addition, there is ineffective erythropoiesis because of an excess of  $\alpha$ -globin chains; these damage the red cell membrane, resulting in cell lysis and an increased breakdown of red cells, which leads to severe anemia.<sup>1</sup>  $\beta$ -Thalassemia major patients are born healthy; however symptoms such as anemia, hepatosplenomegaly, growth retardation, jaundice and bone changes usually develop within the first year of life, thus making regular blood transfusion and iron chelation therapy necessary for survival. The suffering child becomes anemic within a few months of birth and the anemia is so severe that regular transfusions are needed for survival.<sup>2-4</sup>

The patients present with typical facial appearances like high and bulging cheek bones, retraction of the upper lip, protrusion of the anterior teeth and spacing of other teeth, overbite or open-bite, and varying degrees of malocclusion. Prominent cheekbones, frontal bones and jaws imparting a Mongoloid appearance are common findings. This characteristic chipmunk faces is due to marrow hyperplasia in the maxilla and frontal

bossing, profound growth retardation, hepatosplenomegaly, leg ulcers, gallstones, high output congestive cardiac failure and susceptibility to infection. Growth is stunted and puberty is delayed.<sup>5,6</sup>

Multiple blood transfusions in such patients result in iron overload termed hemosiderosis or secondary hemochromatosis due to tissues saturated with iron in reticuloendothelial system and parenchymal cells of the liver, pancreas and heart.<sup>7</sup> Iron overload of tissues, which is fatal if not prevented or adequately treated, is the most important complication of  $\beta$ -thalassemia.<sup>8</sup> Several methods for assessing the body iron overload, like liver biopsies, bone marrow biopsies, are used. However, these procedures are invasive and are not feasible on all occasions. Oral exfoliative cytology is a simple, noninvasive and a safe procedure using the Perl's Prussian blue stain for estimating the iron overload.<sup>9-11</sup> Here we present a 10 year old patient who was referred for dental carious lesions with orofacial deformities like typical mongoloid face, flaring of maxillary teeth and depressed nasal bridge and gave a history of regular blood transfusions for treatment of  $\beta$ -thalassemia since early childhood.

#### Case Report

A 10 year old female patient reported with a chief complaint of decayed tooth with pain in

upper left back region. General examination showed that she was under-built, under-nourished having a short stature with evident icterus and yellow tinged fingernails. The skin was ash grey in color. Head and neck examination revealed, frontal bossing, maxillary expansion, retracted upper lip and saddle nose (Figure 1).



Figure 1: The clinical photograph showing typical mongoloid face in patient with  $\beta$ -thalassemia major.

On further questioning, patient gave a medical history of known case of  $\beta$ -thalassemia major since she was one year old for which she has been undergoing blood transfusion since then, patient had bone marrow aspiration cytology done and reports for iron overload (Figure 2). Intraoral examination revealed bilateral maxillary expansion and grossly decayed tooth #26. The peripheral smear study showed hemolytic anemia favoring Thalassemia. Cytological smear was taken from buccal mucosa and stained with Perl's Prussian blue stain and iron granules were noted in the exfoliated cells (Figure 3). Tooth #26 was treated endodontically and patient is undergoing transfusion every month.

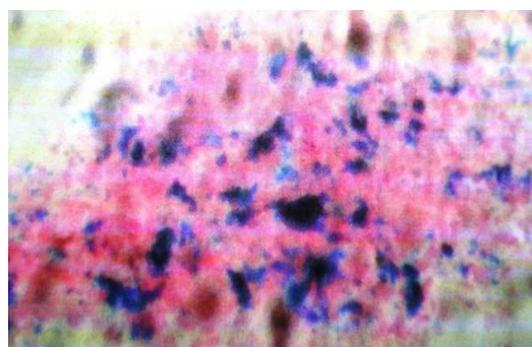


Figure 2: The photomicrograph of Perl's Prussian blue stain positivity in FNAC of bone marrow smear.

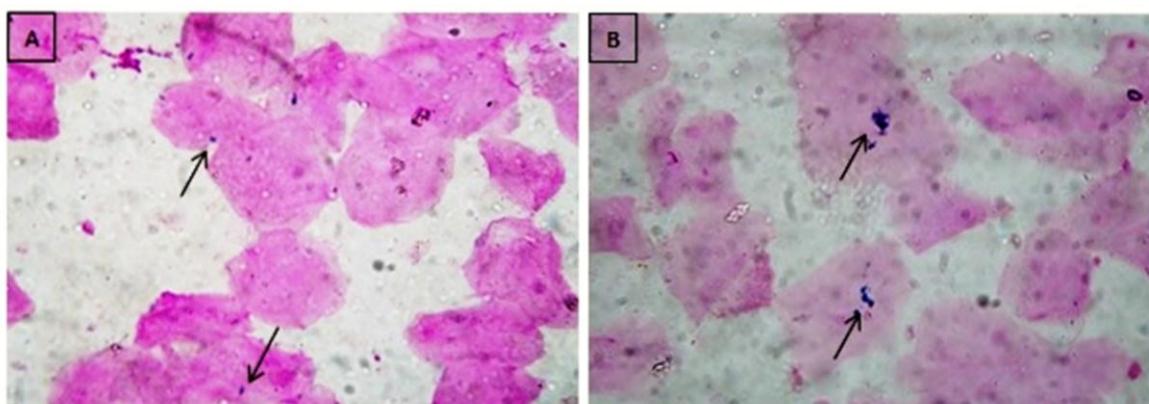


Figure 3: The photomicrograph showing mucosal cells stained with Perl's Prussian blue stain (a) stained and counterstained by neutral red (b) showing positivity for iron overload.

### Discussion

In 1925, Cooley TB and Pearl Lee described a form of severe anemia, occurring in children of Italian origin, associated with splenomegaly and characteristic bone changes.<sup>12</sup>  $\beta$ -thalassemia is the commonest inherited hemoglobinopathy. A high prevalence of  $\beta$ -thalassemia is found in the populations of the Mediterranean region, African continent and in varying frequency in different parts of India, Pakistan,

Bangladesh, Sri Lanka, China and Middle East.<sup>13</sup> Prevalence of  $\beta$ -thalassemia trait varies from 1.0-14.9% in various regions of India.<sup>14</sup>  $\beta$ -thalassemia disorders are a consequence of mutations that impair the normal process of  $\beta$ -globin chain production. In the homozygous state,  $\beta$ -thalassemia [i.e., thalassemia major] causes severe transfusion dependent anemia. In the heterozygous state, the  $\beta$ -thalassemia trait [i.e., thalassemia minor] causes mild to

moderate microcytic anemia.<sup>15</sup> For many patients with  $\beta$ -thalassemia, regular red blood cell transfusions represent lifesaving therapy. Regular blood transfusions have dramatically extended life expectancy in thalassemia major<sup>16</sup> a disease that was once commonly fatal by the age of five.

In  $\beta$ -thalassemia major patient's transfusions help to improve oxygen delivery, suppress the excessive ineffective erythropoiesis and prolong life, but the inevitable side effects, notably iron overload, and usually prove fatal as a result of transfusion iron overload.<sup>5</sup> Iron accumulation in thalassemia and sickle cell anemia patients depends upon the number of blood transfusions given. One unit of blood contains 250ml of red blood cells. Since 1ml of red blood cells contains 1mg of iron, 4 units of blood will contain around 1gm of iron. Signs of clinical toxicity become apparent when body iron reaches 400 to 1000 mg/kg body weight. Transfusion hemosiderosis is the major cause of morbidity and mortality in thalassemia patients.<sup>17</sup>

There are several methods for assessing the body iron overload, like serum ferritin, liver biopsies, bone marrow biopsies, etc. However, these procedures are invasive and are not feasible on all occasions. Oral exfoliative cytology is a simple, noninvasive and a safe procedure for estimating the iron overload by using the Perl's Prussian blue stain.<sup>18</sup> The Perl's Prussian blue reaction is considered to be a classical histochemical reaction which is carried out and is widely applied in the field of hematology. This technique was applied to the exfoliated buccal mucosal cells, considering the fact that the exfoliated cells possibly represent the changes in the underlying parent tissue. The reaction occurs with the treatment of sections in acid solutions of ferrocyanide. Ferric ions (+3) in the tissue combines with the ferrocyanide resulting in the formation of a bright blue pigment called 'Prussian blue' or ferric ferrocyanide. Consequently, the end product of the reaction is such that iron in tissue sections is seen as blue or purple deposits, while other tissue components, such as nuclei and cytoplasm, are highlighted red by the counterstain. As no previous data is available on the Perl's Prussian blue positivity in the exfoliated cells, the positivity for the reaction in our study group was compared with the Perl's reaction positivity in iron overload tissues

like liver biopsies and bone marrow aspiration.<sup>19</sup>

Cytological smears from the exfoliated cells of the buccal mucosa of thalassemia patient who were undergoing repeated blood transfusions were stained with the Perl's Prussian blue technique to demonstrate the presence of an iron overload. Iron positivity in smears stained with Perl's Prussian blue reaction was well appreciated. Hence, we are of the opinion that the oral epithelial cells can reflect the changes in the liver tissues with an iron overload. The buccal smear findings of the present case were in accordance with the findings of the study done by Gururaj and Sivapathasundaram (2004)<sup>17</sup> on ten patients, which revealed positivity for the Perl's Prussian blue reaction in all the ten cases. The present study was also similar to the study which was done by NandaPrasad et al., (2010)<sup>19</sup> in which the exfoliated cells from the buccal mucosa in 65 of the 100 thalassemia patients revealed a positivity for the Perl's Prussian blue reactions.

### Conclusion

Regular blood transfusions are used to avoid growth failure and other pathologic consequences of severe anemia. Iron chelation therapy with deferioxamine 12 hourly given subcutaneous infusions on a daily basis via battery-operated pumps is essential to avoid iron overload. Splenectomy is usually performed if there is increased transfusion requirement from "hypersplenism". Bone marrow transplantations are done in cases where chronic transfusions and chelation are not possible. Considering the simplicity and acceptability of exfoliative cytology method, further studies can establish this non-invasive procedure as an ideal screening and diagnostic tool in all patients undergoing repeated blood transfusions to assess iron overload.

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